



University of Nebraska Medical Center
DigitalCommons@UNMC

MD Theses

Special Collections

5-1-1934

Prevention of rickets

E. E. Anderson

University of Nebraska Medical Center

This manuscript is historical in nature and may not reflect current medical research and practice. Search [PubMed](#) for current research.

Follow this and additional works at: <https://digitalcommons.unmc.edu/mdtheses>



Part of the [Medical Education Commons](#)

Recommended Citation

Anderson, E. E., "Prevention of rickets" (1934). *MD Theses*. 614.

<https://digitalcommons.unmc.edu/mdtheses/614>

This Thesis is brought to you for free and open access by the Special Collections at DigitalCommons@UNMC. It has been accepted for inclusion in MD Theses by an authorized administrator of DigitalCommons@UNMC. For more information, please contact digitalcommons@unmc.edu.

SENIOR THESIS

PREVENTION OF RICKETS

E. E. ANDERSON

UNIVERSITY OF NEBRASKA * COLLEGE OF MEDICINE

APRIL 1934

*

FOREWORD

In compiling this paper
it has not been my en-
deavor to prepare one of
stastical or technical
aspects, but rather one
of practibility and
common usage.

480547

PREVENTION OF RICKETS

HISTORY

Before the main body of this work, Prevention of Rickets, it might be well to give a comprehensive history of the idea of rickets, from ancient times to the epochial era of Glisson.

From allusions in ancient writings, one might infer that rickets was known from earliest times. One author, Sir Thomas Barlow (1) suggest that it is coeval with civilization. Accumulating evidence shows that rickets was unknown in ancient Babylonia, Egypt and India; it is a disease of civilization, associated with growth of industrialism and great towns of Europe. According to Glisson's computations the disease originated in England about the Seventeenth Century.

After stating that the lower animals were subject to rickets, evidenced by remains of apes kept captive in the temples of Thebes, Findlay (2) states, "Should such be indeed the case it would cause us no surprise, as in modern times young monkeys develop rickets." It is recognized that rickets did occur in individual cases, but conditions, giving rise to the present disease, did not exist until late modern times.

By the works of the Ancients, Hippocrates, 460 B.C. and Galen (3) it is more to believed that the disease was

unknown to them. Any such disease, so distinctive would not be missed by these prominent Ancients. Hippocrates divides the curvatures of the spine into three types or classes; the causative factor depending on internal causes, Hippocrates, not unlike present day authors, stresses the importance of environment on disease and not the hereditary factor. Evidence shows that stress only requires to be applied long enough and the response is certain.

As shown by stress the growth of industrialism in the last three or four centuries has produced a race, not improved, but better equipped to survive such environment wherein they have existed. The cleavage between environment and hereditation is not true but remarkably shown by debilitated slum dwelling offsprings developing normally under favorable conditions, while no breast milk or formulae will prevent, of a normal infant, the development of rickets, if such child is kept in damp and sunless rooms. Also, the reverse is true if a child is brought up in open air conditions, exposure to fresh air, and bright sunlight in mild and warm climate, no errors in feedings will produce rickets. Some other states, marasmus, dysentery, or tuberculosis might supervene to carry off the child, but the characteristic rachitic signs will not develop. Hippocrates in "Aphorisms" states the fevers, convulsions, inefficient dentition with obesity in the child with no resemblance to rachitic characteristics is negative evidence of non-existence of the disease at that time.

Findlay (2) believe he has found a true description

of rickets in a passage of the biographer of Hippocrates, Soranus of Ephesus, which runs as follows:

"How should the child be trained in standing and walking?"

"When the infant makes attempts to sit down and stand up, one must assist his movements. For should he show eagerness to sit sooner than is right or too often, he becomes hunched, owing to the backbone bending while as yet the body has no sinews to resist the strain. If he continue to stand up with growing impetuosity, and wish to walk about, his legs commonly become twisted at the thighs."

"Why the majority of Roman children are distorted".

"This is observed to happen more in the neighborhood of Rome than in other places. Some suggest as a reason that the city is undermined by cold waters and that their bodies are easily chilled. Others suggest the frequent sexual intercourse of women, or intercourse taking place after a drunken bout. The truth of the matter lies in inexperience with regard to the rearing of children; for women in the city have not so great a love for their children as to have regard to every particular as the women of purely Greek stock do. If no one oversees the infant's movements his limbs do in the generality of cases become twisted, for the whole weight of the body rests on the legs, and the floor or pavement on which he walks is hard and unyielding, being for the most part laid with stones. When therefore, he rests upon a hard substance, the weight pressing on the limbs is great, and the limbs which bear him up are frail; the limbs must then of necessity give way a little,

since the bones are not yet stiff. Hence, when he first begins to sit he must be propped up by swathings of bandages to counterbalance the ills that can gain the mastery over him, nor must he sit for long at first. As he advances farther to the stage of creeping and standing up for a little, then one should place him up against a wall and leave him alone. But for purposes of making him approach use a chair on wheels. Thus from a gradual common growth of all the members he will practise walking. So much for movement."

The above passage shows clearly what common belief did to the growing infant, loss of motion and free exercise; believing that the infant's limbs should be trained the way that they should grow. Besides discouraging free play of limbs Soranus was also meddlesome in the matter of diet; infant not given food for two days, if any, a little cooked honey, then begin nursing on third day, not by mother but by a nurse for twenty days, then nursing the mother after the first twenty days. In absence of a nurse, a child would have honey and goat's milk for the twenty day period. The practice of swaddling the infant and restraining free movement persisted until 1762 when such practice was vigorously attacked by Jean Jacques Rousseau (4).

Rousseau in a'Emile (4) states that a child immediately being freed of the mother's womb begins to stretch and stir, and to swaddle and constrain the infant checks the "internal impulses", that the infant has gained nothing of being freed of the womb, it hinders the blood circulation, growth

in size and strength and injures the constitution.

This passage shows the attempt to rebel against common belief and that infants so swaddled and retarded would be more liable to rickets and would increase the severity of the attack.

In spite of a common belief the hygiene during the best periods of Greek and Roman civilizations reached the greatest peak in the world's history, surpassing even the extolled cult hygiene of the Egyptians, Babylonians and even the Jews (5). In ancient Nubia and Egypt the skeletons show osteo-arthritis, lipping of articular edges, to complete spine ankylosis and other joints to a degree surpassing that known today. In some six thousand bodies, Dr. Wood Jones (6) found by examination ; syphilis, tuberculosis and rickets so prevalent today. There is, also noted from other surveys, a smaller proportion of infant bodies, but this might be accounted for by less preservative precautions on the frailer bodies. In view of these facts, F. Wood Jones (6) believes the disproportion represents a true mortality index of Egypt; one-fifth the infant mortality than there is today. From works of Mr. Elliot Smith he states with caution that many curved femurs have been found in ruins of ancient Egypt and Nubia but this is refuted by Findlay (2) by a statement that a normal femur may be curved to some extent and that it be justifiable to say that rickets were far more rare than today.

Examination of bones of over four thousand people found in a crypt under a church at Hythe, near Folkestone,

osteo-arthritis of severe type, was found but no rachitic conditions. Even bones of races living along damp shores of Baltic Sea and banks of the Nile show osteo-arthritis to great extent but show little evidence of rachitic disease.

The Roman Hippocrates, Celsus, living in reigns of Augustus and Tiberius in eight books on medicine, deals extensively with caries of bone but does not even hint at rachitic condition.

Rachitic history probably begins with Glisson's publication "De Rachitude" in 1650, published in Latin, republished in 1651, translated into English by Phil Armin (A Treatise of the Rickets, being a Disease common to children printed by Peter Cole at sign of the Printing Press in Cornhill near Royal Exchange 1651.) Glisson lectured on anatomy at Royal College of Physicians, London, but his greatest work was on rickets. Glisson held that rickets had origin in the fluids of the body; (1) that rickets is a cold distemper, (2) that it is moist, (3) that it consisteth in penury or paucity of the spirits, and (4) that it consisteth in the stupification of the spirits.

It was not until 1756 that Cullen, Professor of Medicine in Glasgow, began to undermine fluid origin of disease and to exemplify "solidism". It was the belief of Glisson that rickets was a diseased condition of the blood, chiefly liquid parts. Cullen expounds

the vital solids that is nervous system, and disease depended on the peculiarities of the whole nervous system (7).

Glisson's works have not since been surpassed, as he defined rickets as a separate entity, so complete that not a great deal has been added to our present day knowledge. "Rickets" probably derived from the Middle English word "Wrikken" - to twist, connected with "rick" as "ricked ankle" and "Ricked back". Assisting Glisson by his request were to other Fellows from Royal College of Physicians, who after observation of Glisson's previous understanding of five years study withdrew to preserve unity and harmony of the whole. Studies and observations that Glisson insited other Fellows read and report lead to wide reading of the subject some years before publication by Peter Cole.

Medical piracy existed even at that time as Daniel Whistler published a paper on rickets in 1645, five years previous to Glisson's, but using Glisson's work for the inaugural thesis. The subject could not be disguised from Glisson's work because of his originality, both of study and research, and open clinics with other Fellows. A second notable publication of Whistler appearing in 1649, one year previous to Glisson's, deals in one chapter with rickets, the information of which was undoubtedly borrowed from Glisson.

Glisson discussed at great length rickets, under five headings:

- "I The Dignostical
- II Signs which belong to the disproportional nourishment of the part
- III The signs which belong to the respiration
- IV Those that appertain to the vital influx
- V Certain vagabond and wandering signs"

The anatomical observations are placed under four headings -

"I Anatomical observations, the body not yet being opened, which are outwardly visible upon the first appearance of the naked dead body:

- II The abdomen being opened
- III The stern being withdrawn
- IV The skull being opened."

These headings are followed, both the autopsy and signs, by excellent clinical word pictures which have yet been unsurpassed. Glisson was the first to describe another important infantile disease, infantile scurvy, accurately given and completely disassociated from rickets, of which mention was not made until two hundred years later. Some writers believe that rickets was coexistent with civilization but it was Glisson's idea that rickets was a disease of the rich, bred by luxury, not congenital and mainly a result of environmental conditions operating on the child soon after the birth. In that day and age even Glisson did not recognize any definite therapy or cure but explained the increased or decreased prevalence by the geographical or social environment. In his explanation he advocates the better flourishing country, fertile fields and produce with open air, sunlight and cleanliness of surroundings as this is also true today, prevention rather than therapy remains the most important and greatest division

of rickets. Without so called prevention even today rickets might or might not occur, to allay the uncertainty it is much easier and better medicine to practice prevention rather than therapy.

PREVENTION

Rickets, a disease of early infancy, has not a determined etiological factor; the majority of reports recognize lack or inefficiency of Vitamin D, both in diet and in infant himself as the causative factor. The problem of prevention of rickets presents itself as one of adding or supplying this medium to the infant, before birth to the mother or after birth to the infant, mainly in the diet.

In a quest for a suitable baby food product for prevention of rickets, Barnes (9) used evaporated milk in groups with and without cod liver oil, a breast fed group, and a control group. The trial conducted during the winter months did not show superior results of evaporated milk plus cod liver oil over plain pastuerized milk plus cod liver oil but babies on evaporated milk alone showed a 10% antirachitic increase over breast milk babies and formula babies without cod liver oil.

Practical methods in last few years have developed economical production of irradiated milk for prevention and cure of infantile rickets (10). This problem is one of both public health and commercial practice besides prevention which will be discussed after examining basic conditions.

Huldschinsky's (10) discovery of curative effect of rays of quartz mercury vapor lamp applied to rachitic infants was soon followed by Hess and Steinbock (10) endowing certain food with antirachitic properties. Such properties are now known as Vitamin D synthesized in inert material by a mere exposure of radiant energy. This placed fundamental knowledge available for creation of new agencies for suppression and elimination of infantile rickets which in few exceptions has been presented by adequate quantity of vitamin D. From both American and European sources the efficacy of irradiated fluid or dried milk for prevention of rickets, which gave favorable clinical and biological results but no standardized or basic results as milk is the major material in an infants diet the anti-rachitic content of this article of food is quite desirable. Before production of such irradiated milk considerable work was necessary to commercially prepared in quantities with sufficient value of antirachitis property to warrant commercial production and demand.

Many commercial methods were developed before perfection, or what is now best, was possible on an economical basis; meeting terms to human consumption. After six years of continuous operation and crucial tests the method of film exposure; 0.4 mm in thickness, with rays at varying angles from 60° to 90° at .03 second cycles, exposure not exceeding 16 seconds, meets the required basis. This method is applicable to nearly any plant capacity with very little added equipment. Carbon arcs

of flaming arc type are used and the intensity of radiations applied per unit of time is the factor important in determining the degree of potency. As the synthesis of the antirachitic factor in milk is practically instantaneous, a high rate of energy input per unit of time is necessary and also objectional features develop in extended time exposures. Radiation may be obtained from various sources but only those of constant energy emission and least subject to external influences should be used. The carbon arc under constant electrical conditions, constant voltage and current, is best suited to meet commercial requirements. The age of the lamp does not alter the radiation as the electrodes are replacable when consumed and uniform voltage and current may be easily supplied. Also the visible and ultra-violet radiation may be varied by altering the chemical composition of the carbon electrodes, with uniformity of treatment assured by the development of the recording photo-electric cell ultra-violet ray meter.

With the intake of anirachitic potency almost instantaneous or in a few seconds, vitamin A and C are very little affected. Natural flavor is not impaired or affected to render the milk objectionable. By laboratory and clinical results a definite relationship between energy applied and preventive properties in controlled studies on chickens is not substantially different from infants when calculated in vitamin D per unit weight.

Irradiation of milk by quartz mercury-vapor lamp had been known for some years (Stenboch and Daniells, 1925) and gives the harmful effects of prolonged exposure. After irradiation rigorous tests were compiled to determine the damage if any to vitamin A and by these tests the exposure method of Steenboch and Coward, 1927, (11) was recommended.

By experimental work on rats both treated and untreated milk showed vitamin A present in same quantity by weight and growth comparison and vitamin D increased in irradiated milk by weight and growth comparison on low calcium and low phosphorus diets.

Observations of children fed, treated and untreated milk at alternating months show greater weight gain and less disease susceptibility on the treated milk. The bacterial count is also affected by irradiation, giving very low counts, a few hundred organisms per cc and never above 4000 per cc in spite of previous bacterial count.

From the irradiation experiments, work on rats and finally on children, Nabarro, (11) summarizes his findings as follows:

1. Untreated milk, both whole and skimmed, has very little antirachitic activity. The best sample examined had only 0.11 unit per cc, and this was taken during a time when the cows were receiving the best "summer feed". Three samples taken during the winter months and one taken during a dry month show negligible

antirachitic potency.

2. The antirachitic potency of the milk can be increased enormously by direct irradiation from a quartz mercury-vapour lamp. Where the potency of the untreated milk could be measured, that of the treated milk was increased nine times by an exposure of eight seconds.

3. The capacity for activation of different samples of milk varies.

4. An exposure of 30 seconds had no detectable influence on the vitamin A potency of the milk.

5. The irradiated milk can cure as well as prevent rickets in children and animals, and is of value in other disorders of nutrition, and in other diseases.

6. Irradiation produces a marked decrease in the bacterial count of the milk.

Prevention of rickets in chickens testing antirachitic value of irradiated milk exposed at varying lengths of time,,(12) shows very high percentage of potency in natural whole milk irradiated only a few seconds under suitable conditions as contrasted to the extracted and highly concentrated preparations.

Clinical results obtained from a large number of infants in a health clinic from Department of Health of New York City, (13) who were fed irradiated milk, shows definitely the rachitic protective value. As this test was conducted entirely on colored children and during the months of February and March it was rendered quite severe. With such data the value is summerized thusly;

Milk irradiated under controlled conditions described in this paper and subsequently dried by the Just process, (13) was found to protect even colored infants from rickets during the winter months. Such milk manifested definite curative value in a number of cases, as shown by marked healing in Roentgenograms.

The antirachitic properties of irradiated milk after sufficient experimental prevention on chicken was summarized as follows, (14);

The antirachitic properties of dry milk previously irradiated in fluid form by various carbon arcs and mercury vapor arcs may be accurately determined by the degree of protection against rickets afforded to growing chickens.

In order to prevent chickens from rickets under prescribed conditions, the vitamin D content was calculated to be 1.292 per liter.

Within certain limits, there is a substantial degree of parallelism between the amount of energy applied to the milk and its antirachitic properties as determined by either the standard assay method with rats or its effectiveness in preventing rickets in chickens.

Due to the high incidence percentage of rickets, present in nearly all infants in some degree, prevention and prophylaxis of this disorder has become of public health interest, (15). Due to insufficiency of vitamin D content in foods of infants, both cow's milk and

mother's milk, during rachitic period necessitates irradiation of milk to add such vitamin D potency.

Irradiated milk overshadows cod liver oil by expense, incompatibility to infants taste, laxness, irregular and insufficient dosages as administered by mothers. By reviewing world wide use of irradiated milk one is able to evaluate the wide spread use of such a product.

The use of "cut milk" a half and half mixture of non irradiated and irradiated milk is advocated by Schonen (15) as an appreciable protective measure against rickets. The success of "cut milk" is also reported by Brühl (15) during winter of 1928-29. However Essig (15) recommends that uncut irradiated milk is the only reliable antirachitic food.

On a public health scale Batusch-Marrain (15) commends irradiated milk as potent in combating rickets in preference to dangers of overdosage of other commercial antirachitic products.

By experimental work Batusch-Marrain, keeping children in definite rachitic conditions, (dark unventilated room with milk gruel and no vegetables), reporting severe rickets with two controls same food but in ventilated rooms and increasing amounts of irradiated milk with prevention of rickets, showed the definite value of irradiated milk in prevention of rickets on practically known cases.

Scheer (15) reports favorably on rachitic pro-

phylaxis and cure in premature infants over and above prophylaxis by irradiated ergosterol.

Gyorgy (15) reporting dry irradiated milk as favorable in prevention of rickets, in cases complicated by anemia, eczema, and febrile conditions.

Reichhuber (15) before reporting clinical prevention, calls attention again to Bamberger and Essig and Schonen . Reichhuber, using nineteen ricket free children being fed irradiated milk and twenty-one children as controls, (no irradiated milk) found that one-third of the controls, without irradiated milk, developed rickets, reports favorably on irradiated milk in public health interest.

Weiland (15) from Childrens Clinic at Basle commends American scientists on irradiated dry milk (dryco) recommending it highly for premature infants.

In a German publication Deutsche medizinische Wochenschrift Langestein(15) observing increase of rickets, due to German economic factors, recommends ergosterol but because of overdosages or underdosages, advises irradiated milk.

Working in Edinburgh University, Watson(15) in physiological department on vital food properties reports, " properly irradiated milk has a pronounced curative action on rickets, due to a specific action whereby it's nutritive value is increased".

Medical Research Council(15) reports antirachitic potency of milk greatly increased by irradiation with retention greater than other foods because of freshness which milk must be served.

Hardisty(16) quoting an editorial on "Irradiated Milk" restates that as a preventive factor irradiated milk has a large field due to universality of use and successful activation, both in fluid and dry state without destroying other vital contents. The problem of protecting public interest by controlling rickets has become widely felt, and the use of milk, giving best protection because of ease of preparation and also of high natural calcium and phosphorus content.

After summarizing experimental and preventive properties given before, the article is brought to conclusion by;

The place that has been allotted to irradiated milk in the fight against rickets has been well proven both clinically and experimentally. The fact that is automatic in action and that the antirachitic factor is embodied in the food of the infant insures infestation of sufficient vitamin D for protection against rickets.

The widespread interest along with the multiplicity of articles dealing with the use of irradiated milk both fluid and dry in the prevention and cure of rickets, bids fair to make it of interest to all public health workers as well as members of the medical profession.

The antirachitic potency of human milk is vague but it is definitely known that even though human is superior to cow's milk it will not prevent rickets where rachitic conditions are favorable (17). Clinically the result of feeding vitamin D cow's milk to lactating mothers increases the antirachitic potency, given even in minimum doses shows absence of rickets. In testing five groups of lactating mothers using two as controls, all practically food except controls not receiving vitamin D cow's milk, and refeeding to rats;

controls no breast milk, ordinary breast milk, and vitaminized breast milk, those of the last group showed greater degree of healing by X-ray and also higher Line test(17).

Hence the conclusion that potency of human breast milk can be augmented by adding Vitamin D milk to diet of lactating mother.

The value of ultra-violet rays in prevention of rickets is great but the dosage is not able to be accurately computed. All infants should have fresh air and sunshine exposure, but to definitely say that sunshine alone or ultra-violet rays produced artificially, will prevent rickets does not leave a safety margin. The following paragraphs on such rays in prevention, take up special cases and also difference of potency in different climatic regions.

After various experiments on rats, under ordinary window glass and under special glasses(18), Vitaglass, Vioray glass, and Corning Glass; those under ordinary glass showed rachitic characteristics, while those under special glass little difference in absence of rachitic condition but only 25 to 50 % of those exposed to direct sun rays. Sun rays are definitely known to contain Vitamin D or ultra-violet properties and such properties are obtained only under direct rays or partially under specially constructed glass.

The antirachitic value of ultra-violet rays in sunshine, through celoglass on rats even in winter months is very well demonstrated by Wilder and Vack(19) using general plan of Tisdall and Brown(20), in their experiment but whose main demonstration was to seasonal variation of potency of sunlight. The potency of the rays vary, mostly during winter months, going to the low level during December, January, and greater

part of February, with sharp increase about first of March , and rising to a peak in April and May. The potency being guided by the increase of shorter wave lengths of ultra-vio let rays during those two months.

The experiment of Tisdall and Brown(20) was carried out in Toronto which is in the same latitude as many other of the large northern cities of the United States, therefore applicable to that wide spread region.

Assuming the antirachitic value of ultra-violet rays in sunshine, Stein and Lewis(21) demonstrated the high potency value of Colorado sunshine by prevention of rickets on rats, also the stimulating growth effects of sunshine. By stastic-al reports Colorado is shown to be comparatively free of rickets, this on the basis of smoke and moisture free air rather than direct effect of altitude.

In contradiction to experimental works in Toronto Lewis, Frumess, and Stein(22) by series of experiments on rats show that there is no difference in antirachitic effect of winter and summer sunshine in Colorado due to high percentage of winter sunshine , low humidity and small amount of smbke in the air.

This experiment performed in Toronto has a very practical value, finding the seasonal variation of antirachitic effects of the sun's rays, as the greater part of thickly populated sections all over the world are situated at about the same or even a lower altitude. In using over 5,000 rats over a period of three years, Tisdall and Brown(23) find that a marked antirachitic increase is noted when the sun reaches an altitude above the horizon of 35 degrees or more about

February 15, which is applicable to any locality of such altitude.

Knudsen(24) working on comparative values of different light sources on prevention of rickets in rats finds that the Uviarc operating at 70 volts, takes only 20 seconds daily; General Electric sunlamp, takes 7 minutes; while sunshine varies, June and July from 20 to 30 minutes to January and February sunshine of 270 minutes, carried out of course in rat units. In a foregoing article Knudsen(25) reveals the shortened exposure time necessary for antirachitic effect of ultra-violet rays on exposed body surface of the rats, which would of course correspond to exposed body surface of the child.

After the foregoing articles it is easy to be seen that antirachitic effects of ultra violet rays, both natural and artificial vary, according to exposure, degree of potency, amount of damage present, and also vary according to altitude and climatic conditions.

The balance of this paper will be spent on concentrates of antirachitic potency, the effects of which are most widely advertised and extolled also most abused by advertisers. In the last three four or five years the proprietary concentrates have flooded the markets, have become very popular, widely known and widely used.

In treating on antirachitic concentrates Barnes(26) states the abundance of literature recognizing importance of rickets pathologically and also need of concentrates containing proper potency in small doses. The optimum preventive dosage recognized by majority of clinicians(27) was three(3)

teaspoons(1500-20000slo rat units or 150-200 Steenbock units) per day. It is generally recognized that the curative dosage is about two to three times that of the prophylactic dosage, but Hees(23) recommends in extreme cases dosages up to ten teaspoonfuls per day.

Numbered among the antirachitic agents regarded as concentrates are: first, viosterol, activated ergosterol; second, concentrates of cod liver oil; third, cod liver oils with viosterol; fourth, fish liver oils, much richer in Vitamin A and D than poor cod liver oils; and fifth, the combination of carotin for Vitamin A with viosterol or with cod liver oil.

Viosterol(irradiated ergosterol) popular last few years, made by activating inert ergosterol provides a concentrate easy to administer in small doses. At first it was thought that viosterol contained equal potency , unit for unit with cod liver oil for prevention and cure of rickets, but after later studies this was not found to be so; and the potency of viosterol was stepped up to meet the concentrate requirement. In spite of popularity it is felt by some that viosterol is not superior to natural Vitamin D of cod liver oil in rachitic condition. Also the lack of Vitamin A in viosterol formed a common objection but this has been changed by addition of fish liver oil to viosterol, making concentrate of both Vitamin A and D. Certain fish liver oils, much richer in Vitamin A and D than cod liver oil, among these are halibut liver oil and burbot liver oil. Halibut liver oil known as "haliver oil" contains 100 times the Vitamin A and 15 to 20 times the Vitamin D in plain cod liver oil, but this objection

was offered that an infant would obtain sufficient Vitamin A but not enough Vitamin D. In an effort to balance the amount of both Vitamin A and D, increased dosage was given, but that would cause overdosage of Vitamin A, then to offset that angle viosterol was added, but as yet has not been proven justifiable.

Many commercial cod liver oil concentrates have been available for some years but after assaying by reliable groups only a few have been found to contain therapeutic quantities of Vitamin A and D as prescribed. Vitamin concentrates in tablets were found to lose potency and those in oil solution or in capsules were most reliable in retaining stated potent units. In experimenting on cod liver oil Dr. F.W. Heyl of Upjohns was the first; but by group tests after increase of weight growth and potential antirachitic properties of blood calcium and phosphorus soon dropped back to former level and severe rickets was evidenced in those not continuing treatment after curative effects were pronounced. Vitamin D milk homogenized with Zuckers cod liver oil concentrate meets the Vitamin D requirement but not the Vitamin A later found best given in whole milk which contains necessary amount of Vitamin A.

In comparing preventive antirachitic value of cod liver oil and irradiated ergosterol, D.J. Barnes, Brady, and James (28) studied a controlled group of infants; some given cod liver oil, some irradiated ergosterol, some combination of cod liver oil and irradiated ergosterol, and a number without any antirachitic agent. These infants were not especially selected, they were taken in rotation as they came into clinic

and assigned to one of the four groups. A safe optimum dosage of cod liver oil was given , three teaspoonfuls per day, regulating in comparison the dosage of irradiated ergosterol. The accurate determination of blood calcium and phosphorus were made as well as roentgen examinations of the long bones of the body. The infants were weighted regularly and received adequate diets, those of rachitic start were used as controls until rickets or other infections might jeopardize their permanent health, they were then taken out of the series and put under proper diet and medication. After the experiment was ran December 1928 to April 1929 cod liver oil was found to have prevented or cured rickets in 98% of the cases, dosage of three(3) teaspoonfuls daily(1400 rat units of Vit. D), the cod liver oil and irradiated~~er~~ ergosterol prevented or cured 98% of the cases, dosage three teaspoonfuls daily (3,750 rat units Vit.D daily), that cod liver oil in daily dosage of only 1,400 rat units prevented rickets more than irradiated ergosterol at 1,250 rat units of Vit. D per day which prevented or cured only 44% of the cases studied; and that breast and formula fed infants varied little , but evidence showed greater need in colored infants. With information of vitamin content of various natural products and possibility of irradiating food substances, it appeared possible to standardize the uniform antirachitic dosage of both cod liver oil and viosterol. After experiments on rats and correlating conclusions of Barnes, Brady, and James(28), Holmes and Piggot (29) found variance of potency in different brands of viosterol. "Either the recommended prophylactic dose of viosterol is too small to prevent rickets or rickets is not due to a deficiency of

Vitamin D alone. We are inclined to believe that the second of these possibilities is true". Determination of six brands of irradiated ergosterol--Viosterol 100D did not show uniform antirachitic value, that is, various brands do not possess one hundred times the antirachitic value of standard cod liver oil. It was also found that viosterol 100D, possessing highest antirachitic activity of those tested, had less than sixty times the antirachitic activity of the best cod liver oil tested. In spite of the higher value of low grade viosterols as compared to the better cod liver oils, it is recognized that irradiated ergosterol has only the antirachitic function whereas the cod liver oil possesses this and is also rich in vitamin A.

In a study of the potency of various cod liver oil and viosterol units on controlled groups of infants, De Sanctis and Craig (30) reach similar conclusions as do Barnes, Brady, and James (28) only to more detail of units potency. Of cases studied; cod liver oil in dosage of three teaspoonfuls a day (170 Steenbock Vitamin D Units) prevented rickets in 97% of 100 cases; Viosterol 100 D given in 10 drops daily doses (300 Steenbock units) prevented rickets in 77% of cases; viosterol 250 D in 10 drop daily doses (750 Steenbock vitamin D units) prevented rickets in $81\frac{1}{2}\%$ of cases; viosterol in 500 D given in 10 drop doses (1500 Steenbock vitamin D units) prevented rickets in 90% of the cases studied; and cod liver oil in concentrate tablet form given in doses of three tablets daily (150 Steenbock vitamin D units) prevented rickets in $92\frac{1}{4}\%$ of the cases. From above results it is noted that only 170 units of vitamin D are necessary to prevent rickets and it is expressed that rickets is not a disease of vitamin D alone but also of vitamin A and possibly other factors play an important part.

In a study of antirachitic potency of irradiated ergosterol on pregnant women, premature infants and newborns, Moore Dennis, and Phillips(31) used Mead's activated ergosterol and also climatic variation in determination that it was impossible to give enough cod liver oil, in the Pacific Northwest to prevent or cure rickets. In pregnant women given 6 drops of Mead's viosterol daily it was found that they kept an unusual sense of well being during pregnancy and delivered normally without difficulty, well formed and vigorous infants. In this article it is also reported that newborns receiving 20 drop drops of viosterol daily from birth are superior to those not receiving it, that twins and prematures should receive 30 drops daily, and active rickets 20 to 30 drops daily with no harmful effects evidenced from dosages up to 50 drops daily.

Due to the accepted fact that premature infants are prone to develop rickets, E.W.May(32) instituted experimental studies to establish adequate preventative measures. Due to amount needed in preventative therapy cod liver oil would not be well tolerated because of high fat content, but viosterol, on controlled premature infants was found to prevent rachitic formation as well as promote general well being, increase weights, increase appetites, reduce infection susceptibility, and reduce death percentages, without gastric distress. The dosage of viosterol should start within 24 hours of birth, 45 to 60 drops after first ten days to six or eight weeks and gradually reduce dosage to 20 or 30 drops daily. The accurate dosage is not well established, as it depends on the infant and degree of control with suggestion of minimal dose of 30 drops and maximal dose of 60 drops as an effective range in

prevention of rickets in premature infants.

The reports of the council on Pharmacy and Chemistry (27) states the varying recommended dosages of various cod liver oils. The U. S. Pharmacopeia permits the claim of 50 vitamin A units per gram but no standard official method of assay for vitamin D has been adopted. The claims of Vitamin D units of various oils differ but in vitamin A the units guaranteed range from 500 to 1000, none less than 500. The Council in an effort to ascertain the amount of Cod liver oil to be administered under ordinary conditions, sent an inquiry to nineteen different prominent Pediatricians; with return abstracts the dosages were expressed wholly in vitamin D content and not to vitamin A which probably plays a large part in the antirachitic factor. As stated before the optimum dosage of cod liver oil was arrived at three (3) teaspoonfuls (12 c.c.) daily with due allowance for variations in potency, for factors of age, rate of growth, race, diet, sunlight, and climate, and intercurrent infections. The three teaspoonfull dosage represents the best standard that can be established at present, bearing in mind that, Hess (27) states, "no antirachitic agent is absolutely able to prevent rickets if the disorder is judged by the most delicate clinical criteria."

Recognizing the available number of antirachitics Hess(33) evaluates five reliables; first, cod liver oil natural product; second, direct irradiation to the body; third, irradiated food, mainly milk; fourth, irradiated basic substances as ergosterol; and fifth, irradiated yeast. The adoption of one or more of these for community eradication of

rickets depends on the cost, popularity, palatability, and other non-medical considerations. In protection irradiated milk requires small number of rat units(35 to 40 daily) and viosterol requires the largest number, as compared to clinical computation irradiated milk requires only 20-24 ounces daily for protection, being automac and inexpensive. The present rating method of antirachitic units is misleading, in that each type of agent must be appraised for itself, therapeutic units determined and then expressed in rat units.

In conclusion of this article it need not be discussed at great length the antirachitic products aforementioned; cod liver oil at optimum dosage of three(3) teaspoonfuls daily seems to be more to common usage, adopted to the ordinary case where prevention is desired. Irradiated milk as an agent of antirachitic properties remains as one of general public health usage, applicable also to ordinary cases, but not to be substituted for other available products when potency is not definitely determined. Ultra-violet rays in preventive measures remains one of undetermined quantities, mainly in direct irradiation by the sun, due to climatic and seasonal differences, and also in irradiation by special lamps unless accurately computed from beginning to end; special lamps present problems of economic importance, both to the one requirement of equipment and to the patient in expense of treatments. Viosterolis of importance in supplying to the expectant mother, premature infants, and newborn; minimum dosage to infants from 20 to 30 drpps daily to maximum dosage up to 60 drops daily in extreme cases.

BIBLIOGRAPHY

- (15) Auerbacher, Louis J.-- Prevention and Cure of Rickets
Through Irradiated Milk p.383
Medical Journal and Record - Vol. 138-- 1932
- (1) Barlow, Sir Thomas--
Keating's Cyclopedia of Diseases of Children- Vol.II
- (9) Barnes, Donald J.-- Effect of evaporated Milk on the Incidence of Rickets in Infants-- p; 397
Journal Michigan State Medical Society--Vol.31--1931
- (26) Barnes , D.J. --Antirachitic Concentrates--p.242
Journal Michigan State Medical Society-- Vol. 32-1932
- (28) Barnes,D.J.
Brady,M.J.
James,E.M.---Comparative Value of Irradiated Ergosterol
and Cod Liver Oil as a Prophylactic Antirachitic Agent When Given in Equivalent Dosages
According to Rat Units of Vitamin D--p.45
American Journal Diseases Of Children Vol. 39 1930
- (8) Bartholemwe, Sir T.-- History of the First Treatise in Rickets p.863
St. Bartholemew's Hospital Reports Vol. XX-- 1884
- (7) Buckle, William
Civilization in England-- Vol. III London 1904
- (17) Bunker, JohnW.M.
Harris, Robert S.
Eustis, Richard S.--- Antirachitic Potency of the Milk of Human Mothers Fed Previously on Vitamin D
Milk of the Cow---- p. 313
New England Journal of Medicine-- Vol 208--1933

- (27) Council of Pharmacy and Chemistry- Reports of the
Council on Average Optimum Dosage
of Cod Liver Oil p. 316
Journal of the American Medical Association Vol.93 1933
- (30) De Sanctis, Adolph G.
Graig, John Dorsey -- Study of Prophylactic Value of Various Antirachitic Agents.p.1133
New York State Journal of Medicine Vol31--1931
- (3) Dick, J. Lawson -- History of Rickets
Rickets by J. Lawson Dick.
- (2) Findlay, Richard F.--Social and Economic Factors in the
Causation of Rickets.
Introductory Historical Survey To A Study of Social
and Economical Conditions. London 1918.
- (16) Hardisty, Ester B.--Sunshine and Irradiated Milk Therapy
To Reduce High Incidence of Rickets
Page 549
Archives of Pediatrics Vol. 50, 1933.
- (33) Hess, Alfred F.
Lewis, J. M. --An Appraisal of Antirachitics In Terms
Of Rat and Clinical Units Page 181.
Journal American Medical Association-Vol. 101, 1933.
- (29) Holmes, Arthur D.
Pigott, Madeline G.--Relative Antirachitic Activity of
Cod Liver Oil and Irradiated Ergosterol.
(Viosterol) Page 220.
New England Journal of Medicine. Vol. 203, 1930
- (6) Jones, Dr. F. Wood
Smith, G. Elliot --Cairo and General Pathology-Page 19
Archaeological Survey of Nubia-Vol. 2, 1907-08.

- (24) Knudson, Arthur--Comparative value of Several Light Sources for Cures and Prevention of Rickets. Page 531.
American Journal Diseases of Children. Vol.42, 1931.
- (25) Knudson, Arthur--Exposure Time of Ultra-Violet Rays for Antirachitic Effect. Page 524.
American Journal Diseases of Children. Vol. 42, 1931.
- (22) Lewis, R. C.
Frumes, G. M.
Stein, H. B.--A Comparison of the Antirachitic Effects of Winter and Summer Sunshine in Colorado. P.71.
American Journal Diseases of Children. Vol. 41, 1931.
- (32) May, Earl W.--Prevention of Rickets in Premature Infants by the Use of Viosterol 100D Page 1376
Journal American Medical Association. Vol. 96, 1931.
- (31) Moore, C. Ulyssis
Dennis, H. G.
Phillips, B. J.--Antirachitic Action of Activated Ergosterol. Page 26.
Northwest Medicine. Vol. 29, 1930
- (11) Nabarro, David--The Irridation of Milk for the Increasing of Its Antirachitic Potency.
Page 129.
Lancet Vol. 1- Jan. 1930.
- (4) Rousseau, "Emile Ou De l'Education.
Citoyen de Geneve Amsterdam 1762.
- (21) Stein, Hermann B.
Lewis, Robert C. Rickets; The Comparatively High Value of Colorado Sunshine in its Prevention. P.63
American Journal Diseases of Children. Vol.41, 1931.

- (5) Sudholf, Prof. Karl Hygienic Idea and Its Manipulation
in World History.

Annals of Medical History-Vol. 2, 1917.

- (10) Supplee, G. C.- Ph. D. Antirachitic Activation of
Milk by Direct Irridation with Ultra-Violet Rays
Page 225.

American Journal Public Health

- (14) Supplee, G. C.
Bend, H.
Dorcas, M. C. Irradiated Milk; The Amount of Energy
Required to Prevent Rickets in Chickens. P63

Journal Biological Chemistry. Vol. 97 1932.

- (13) Supplee, G. C.
Dorcas, M. J.
Hess, A. F. Antirachitic Activation of Milk. P 116.

Journal Biological Chemistry. Vol. 94, Jan. 1932.

- (12) Supplee G. C.
Flanigan
Kohlenberg
Hess--Comparative Antirachitic Value of Irradiated Milk
and Milk Derivatives. Page 783.

Journal of Biological Chemistry. Vol. 91, 1931.

- (18) Tisdall, F. F.
Brown, Alan -- Antirachitic Value of Suns Rays Through
Various Special Window Glasses. P.742.

American Journal Diseases of Childred Vol. 34, 1927.

- (20) Tisdall, F. F.
Brown, Alan----Seasonal Variation of the Antirachitic
Effect of Sunshine Page 721

American Journal Diseases of Children Vol34, 1927.

- (23) Tisdall, F. F.
Brown, Alan--Seasonal Variation in the Antirachitic

Effect of Sunshine Page 1147.

American Journal Diseases of Children Vol.42 , Part 2
1931

- (19) Wilder, Theodore S.
Vack Christine--Antirachitic Effect of Winter Sunshine

Through Celoglass. Page 930.

American Journal Diseases of Children. Vol 39, 1930.